

REMARKS

Reconsideration is requested.

The Advisory Action of February 7, 2007 indicates that the Amendment of December 28, 2006 has been entered and that the previously submitted reference of Eum et al has not been considered.

The attached RCE is being filed to ensure consideration of Eum et al. Acknowledgement of consideration of the reference by return of an initialed copy of the attached PTO 1449 Form listing the same, pursuant to MPEP § 609, are requested.

The Examiner is requested to acknowledge receipt of the certified copy of the priority document filed January 26, 2004. A review of the PTO PAIR IFW by the undersigned confirms that the previously-filed certified copy of the priority document is contained therein. The undersigned has previously requested the Examiner's acknowledgement of receipt of the certified copy of the priority document on January 26, 2004, January 19, 2006, and September 27, 2006.

Claims 1 and 2 have been further amended to clarify the recitation with regard to the fragment of the claims. No new matter has been added.

The Section 112, first paragraph, rejection of claims 1, 2, 10, 43 and 44 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the previously-submitted evidence as well as the following comments.

The applicants urge the Examiner to appreciate that the presently claimed invention relates to a method for inhibiting KDR/Flk-1 signal transduction in endothelial cells, and a method for inhibiting cell growth of endothelial cells, each of which involves

contacting the cells with an anti-1175-tyrosine phosphorylated KDR/Flk-1 antibody (anti-PY1175 antibody).

The Examiner asserts that the previously-submitted evidence

“require that the antibody be injected into the cell or transfected into the cell to achieve the observed effects. The techniques are not applicable for *in vivo*/therapeutic use in which the antibody must be able to contact antigen presented on the surface of the cell.” See page 2 of the Office Action dated August 28, 2006.

The previously-submitted evidence (Declaration of Dr. Shitara submitted May 30, 2006) demonstrates that the cell growth of endothelial cells is inhibited by mixing the anti-PY1175 antibody with Chariot and contacting it with vascular cells. The Examiner will appreciate that Chariot is also known as PEP-1 peptide having 21 amino acid residues, and is known to be a carrier peptide which transports a full-length protein *in vivo* and *in vitro*. See Abstract of attached Won Sik Eum et al, *Free Radical Biology & Medicine* Vol 37, No. 10, pp. 1656-1669 (2004)). The attached Eum et al further teaches that a fused polypeptide of antioxidant enzyme Cu,Zn-superoxide dismutase (SOD) and PEP-1 peptide is transduced *in vivo* in the skin (Fig 6) and in the neuronal cells of an ischemia animal model (Fig 7). The attached document was previously submitted as evidence in response to the Examiner's comments and as such is believed to have been submitted in a timely manner. See MPEP Section 609.05(c).

Consideration of the attached is again requested.

It will therefore be clear to one of ordinary skill in the art that cell growth of endothelial cells is inhibited *in vivo* by administering to an animal a mixture of anti-PY1175 antibody having an *in vitro* effect with the known PEP-1 peptide (Chariot).

The claims are submitted to be supported by an enabling disclosure and withdrawal of the Section 112, first paragraph, rejection of the claims is requested.

The objection to claim 10 is obviated by the amendments filed December 28, 2006. Withdrawal of the objection is requested.

The Section 112, first paragraph, rejection of claims 43 and 44 is obviated by the attached English translation of the previously-submitted deposit receipt. The applicants confirm by the attached Budapest Treaty deposit receipt that hybridoma KM3035 has been deposited as FERM BP-7729 under the provisions of the Budapest Treaty. The applicants confirm that all restrictions on the release of the deposited material will be removed upon the grant of the claims in a patent based on the present application. Withdrawal of the Section 112, first paragraph, rejection of claims 43 and 44 is requested.

The Section 112, first paragraph, rejection of claims 1, 2, 10, 43 and 44 is obviated by the previously-filed amendment. Withdrawal of the rejection is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested.

The Examiner is requested to contact the undersigned in the event anything further is required in this regard.

SHIBUYA, et al.
Appl. No. 10/763,276
Monday, April 30, 2007
SECOND AMENDMENT AFTER FINAL REJECTION

Respectfully submitted,

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